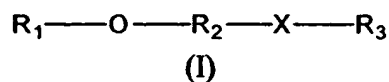


Claims

What is claimed is:

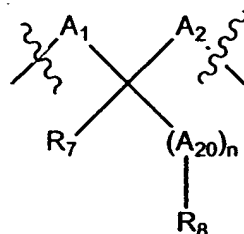
1. A compound of formula (I):



wherein:

R_1 is aryl;

R_2 is a group of formula (II):



wherein

A_1 , A_2 , and A_{20} are each independently alkylene or substituted alkylene;

n is 0 or 1;

R_7 is hydrogen, alkyl, or substituted alkyl;

R_8 is $\text{NR}_{10}\text{R}_{11}$, wherein each of R_{10} and R_{11} is independently hydrogen, alkyl, or substituted alkyl; and

X is oxygen and R_3 is aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkyl, or substituted alkyl; or

X is a direct bond and R_3 is an N-linked heteroaryl or an N-linked heterocycle;

wherein any aryl of $\text{R}_1\text{--R}_3$ can optionally be substituted with from 1 to 5 substituents R_g ; wherein each R_g is independently selected from the group consisting

of hydroxy, alkyl, substituted alkyl, alkoxy, cycloalkoxy, substituted cycloalkoxy, methanediol, ethanediol, cycloalkyl, substituted alkyl, substituted alkoxy, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxy, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heteroaryl, heteroaryloxy, heterocyclic, heterocyclooxy, heteroaryl and trihalomethyl;

and wherein any heteroaryl of R_2 - R_3 can be optionally substituted with 1 to 5 substituents R_h , wherein each R_h is independently selected from the group consisting of hydroxy, alkyl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, substituted alkyl, arylalkyl, heteroarylalkyl, heterocyclealkyl, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxyl, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heterocyclic, and trihalomethyl.

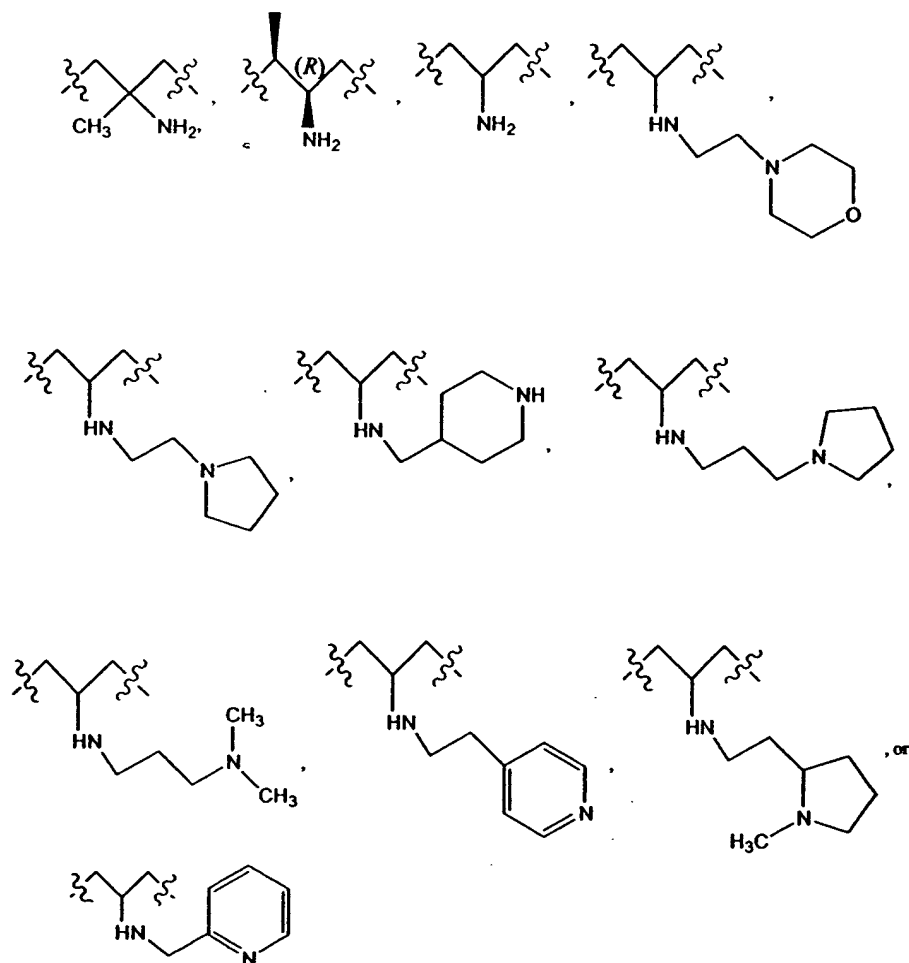
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 wherein R_1 is aryl optionally substituted with one or more halo or alkyl.
3. The compound of claim 1 wherein R_1 is 2-methylphenyl, 2-chloro-6-methylphenyl, 2,4,6-trifluorophenyl, 2,6-dimethylphenyl, or 2,4-dimethylphenyl.
4. The compound of claim 1 wherein A_1 is methylene or 1,1-ethanediyl, and A_2 is methylene.
5. The compound of claim 1 wherein R_7 is hydrogen or methyl.
6. The compound of claim 1 wherein R_8 is amino.
7. The compound of claim 1 wherein n is 0.

8. The compound of claim 1 wherein R_8 is $NR_{10}R_{11}$; and R_{11} is heterocyclealkyl, heteroarylalkyl, or alkyl.

9. The compound of claim 1 wherein R_8 is $NR_{10}R_{11}$; R_{10} is hydrogen; and R_{11} is 2-morpholinoethyl, 2-(pyrrolidin-1-yl)ethyl, 4-piperidinylmethyl, 3-(*N,N*-dimethylamino)propyl, 2-(1-methyl-pyrrolidin-2-yl)ethyl, 2-(4-pyridyl)ethyl, or 3-(pyrrolidin-1-yl)propyl.

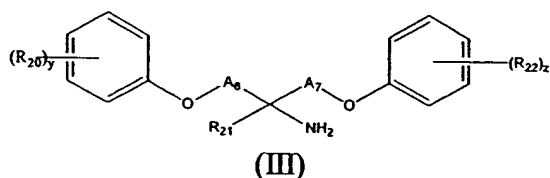
10. The compound of claim 1 wherein R_2 is a group of the formula:



11. The compound of claim 1 wherein X is a direct bond and R₃ is 3,5-dimethylpyrazol-1-yl, 2-phenylimidazol-1-yl, 2-ethylimidazol-1-yl, 1-benzimidazolyl, 4-(methoxycarbonyl)imidazol-1-yl, 4-methyl-2-ethylimidazol-1-yl, or 4-phenyl-1-imidazol-1-yl.

12. The compound of claim 1 wherein X is oxygen and R₃ is 3,5-dichlorophenyl, 2-thien-2-ylethyl, 4-methylbenzyl, 4-methoxyphenethyl, 4-methylphenethyl, 3-(benzyloxy)propyl, 2-[3-(6-methylpyrid-2-yl)propyloxy]ethyl, 2-(ethoxy)ethyl, 3-(ethoxy)propyl, benzyl, cyclopropylmethyl, 4-(butoxy)benzyl, 2-(cyclohexyloxy)ethyl, pentyl, 3-phenylpropyl, 2-[2-(ethoxy)ethoxy]ethyl, 2-phenylbenzyl, 3-(*N,N*-dimethyl)propyl, *tert*-butyl, 2-(phenoxy)ethyl, 2-(pyrid-4-yl)ethyl, 2-methylphenyl, 2-chloro-6-methylphenyl, 2,4,6-trimethylphenyl, 2,6-dimethylphenyl, 2,4-dimethylphenyl, 3,4-methylenedioxybenzyl, 3-(pyrid-3-yl)propyl, or 4-(*N,N*-dimethyl)phenethyl.

13. The compound of claim 1 which is a compound of formula (III):



wherein:

A₆ and A₇ are each independently alkylene or substituted alkylene;

each R₂₀ is independently halo, alkyl, substituted alkyl, aryl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR₄R₅, or CO₂R₆;

R₂₁ is hydrogen, alkyl, or substituted alkyl;

each R₂₂ is independently halo, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkoxy, substituted alkoxy,

cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR_4R_5 , or CO_2R_6 ;

y is 0, 1, 2, 3, 4, or 5;

z is 0, 1, 2, 3, 4, or 5; and

$\text{R}_4\text{-R}_6$ are each independently hydrogen, alkyl, or substituted alkyl;

wherein any aryl of A_6 , A_7 , $\text{R}_{20}\text{-R}_{22}$ and $\text{R}_4\text{-R}_6$ can optionally be substituted with from 1 to 5 substituents R_g ; wherein each R_g is independently selected from the group consisting of hydroxy, alkyl, substituted alkyl, alkoxy, cycloalkoxy, substituted cycloalkoxy, methanediol, ethanediol, cycloalkyl, substituted alkyl, substituted alkoxy, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxy, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heteroaryl, heteroaryloxy, heterocyclic, heterocycloxy, heteroaryl and trihalomethyl;

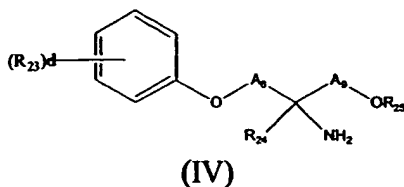
and wherein any heteroaryl of A_6 , A_7 , $\text{R}_{20}\text{-R}_{22}$ and $\text{R}_4\text{-R}_6$ can be optionally substituted with 1 to 5 substituents R_h , wherein each R_h is independently selected from the group consisting of hydroxy, alkyl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, substituted alkyl, arylalkyl, heteroarylalkyl, heterocyclealkyl, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxyl, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heterocyclic, and trihalomethyl.

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13 wherein A_6 is methylene or 1,1-ethanediyl and A_7 is methylene.

15. The compound of claim 13 wherein R_{21} is hydrogen or methyl.

16. The compound of claim 1 which is a compound of formula (IV):



wherein:

A_8 and A_9 are each independently alkylene or substituted alkylene;

each R_{23} is independently halo, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR_4R_5 , or CO_2R_6 ;

R_{24} is hydrogen, alkyl, or substituted alkyl;

R_{25} is alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, or heterocycle;

d is 0, 1, 2, 3, 4, or 5; and

R_4 - R_6 are each independently hydrogen, alkyl, or substituted alkyl;

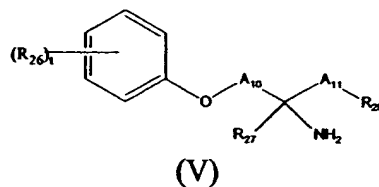
wherein any aryl of A_8 , A_9 , R_{23} - R_{25} and R_4 - R_6 can optionally be substituted with from 1 to 5 substituents R_g ; wherein each R_g is independently selected from the group consisting of hydroxy, alkyl, substituted alkyl, alkoxy, cycloalkoxy, substituted cycloalkoxy, methanediol, ethanediol, cycloalkyl, substituted alkyl, substituted alkoxy, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxy, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heteroaryl, heteroaryloxy, heterocyclic, heterocycloxy, heteroaryl and trihalomethyl;

and wherein any heteroaryl of A_8 , A_9 , R_{23} - R_{25} and R_4 - R_6 can be optionally substituted with 1 to 5 substituents R_h , wherein each R_h is independently selected from the group consisting of hydroxy, alkyl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, substituted alkyl, arylalkyl, heteroarylalkyl, heterocyclealkyl, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy,

carboxyl, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heterocyclic, and trihalomethyl.

or a pharmaceutically acceptable salt thereof.

17. The compound of claim 16 wherein A_8 is methylene and A_9 is methylene.
18. The compound of claim 16 wherein R_{24} is hydrogen or methyl.
19. The compound of claim 16 wherein R_{25} is 2-morpholinoethyl, 2-(pyrrolidin-1-yl)ethyl, 4-piperidinylmethyl, 3-(*N,N*-dimethylamino)propyl, 2-(1-methylpyrrolidin-2-yl)ethyl, 2-(4-pyridyl)ethyl, 3-(pyrrolidin-1-yl)propyl, 2-[2-(ethoxy)ethoxy]ethyl, 3-(ethoxy)propyl, benzyl, cyclopropylmethyl, 2-(1-methylpyrrolidin-2-yl)ethyl, 2-(pyrid-4-yl)ethyl, 3-(pyrrolidin-1-yl)propyl, pentyl, 3-phenylpropyl, 3,4-(methylenedioxy)benzyl, 3-(pyrid-3-yl)propyl, 4-(*N,N*-dimethyl)phenethyl, 4-(butoxy)benzyl, 2-(cyclohexyloxy)ethyl, 3,5-dichlorophenyl, 2-(thien-2-yl)ethyl, 4-methylbenzyl, 2-phenylbenzyl, 3-(*N,N*-dimethyl)propyl, *tert*-butyl, 2-(phenoxy)ethyl, 2-[3-(6-methylpyrid-2-yl)propyloxy]ethyl, 2-(ethoxy)ethyl, 4-methoxyphenethyl, 4-methylphenethyl, or 3-(benzyloxy)propyl.
20. The compound of claim 1 which is a compound of formula (V):



wherein:

A_{10} and A_{11} are each independently alkylene or substituted alkylene;

each R_{26} is independently halo, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR_4R_5 , or CO_2R_6 ;

R_{27} is hydrogen, alkyl, or substituted alkyl;

R_{28} is an N-linked heteroaryl or an N-linked heterocycle;

t is 0, 1, 2, 3, 4, or 5; and

R_4 - R_6 are each independently hydrogen, alkyl, or substituted alkyl;

wherein any aryl of A_{10} , A_{11} , R_{26} - R_{28} and R_4 - R_6 can optionally be substituted with from 1 to 5 substituents R_g ; wherein each R_g is independently selected from the group consisting of hydroxy, alkyl, substituted alkyl, alkoxy, cycloalkoxy, substituted cycloalkoxy, methanediol, ethanediol, cycloalkyl, substituted alkyl, substituted alkoxy, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxy, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heteroaryl, heteroaryloxy, heterocyclic, heterocyclooxy, heteroaryl and trihalomethyl;

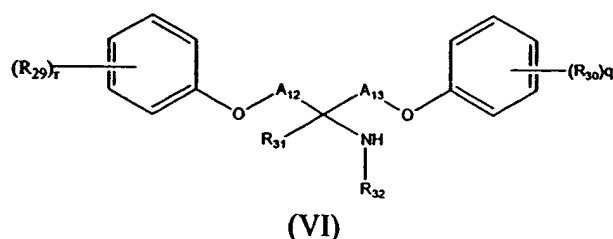
and wherein any heteroaryl of A_{10} , A_{11} , R_{26} - R_{28} and R_4 - R_6 can be optionally substituted with 1 to 5 substituents R_h , wherein each R_h is independently selected from the group consisting of hydroxy, alkyl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, substituted alkyl, arylalkyl, heteroarylalkyl, heterocyclealkyl, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxyl, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heterocyclic, and trihalomethyl.

or a pharmaceutically acceptable salt thereof.

21. The compound of claim 20 wherein A_{10} is methylene and A_{11} is methylene.
22. The compound of claim 20 wherein R_{27} is hydrogen or methyl.

23. The compound of claim 20 wherein R_{28} is 3,5-dimethylpyrazol-1-yl, 2-phenylimidazol-1-yl, 2-ethylimidazol-1-yl, 1-benzimidazolyl, 4-(methoxycarbonyl)imidazol-1-yl, 4-methyl-2-ethylimidazol-1-yl, or 4-phenyl-1-imidazol-1-yl.

24. The compound of claim 1 which is a compound of formula (VI):



wherein:

A_{12} and A_{13} are each independently alkylene or substituted alkylene;

each R_{29} is independently halo, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR_4R_5 , or CO_2R_6 ;

each R_{30} is independently halo, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, heterocycle, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, trifluoromethyl, cyano, nitro, hydroxy, NR_4R_5 , or CO_2R_6 ;

R_{31} is hydrogen, alkyl, or substituted alkyl;

R_{32} is alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, or heterocycle;

r is 0, 1, 2, 3, 4, or 5;

q is 0, 1, 2, 3, 4, or 5; and

R_4 - R_6 are each independently hydrogen, alkyl, or substituted alkyl;

wherein any aryl of A_{12} , A_{13} , R_{29} - R_{32} and R_4 - R_6 can optionally be substituted with from 1 to 5 substituents R_g ; wherein each R_g is independently selected from the group consisting of hydroxy, alkyl, substituted alkyl, alkoxy, cycloalkoxy, substituted cycloalkoxy, methanediol, ethanediol, cycloalkyl, substituted alkyl, substituted alkoxy, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxy, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heteroaryl, heteroaryloxy, heterocyclic, heterocyclooxy, heteroaryl and trihalomethyl;

and wherein any heteroaryl of A_{12} , A_{13} , R_{29} - R_{32} and R_4 - R_6 can be optionally substituted with 1 to 5 substituents R_h , wherein each R_h is independently selected from the group consisting of hydroxy, alkyl, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, substituted alkyl, arylalkyl, heteroarylalkyl, heterocyclealkyl, substituted cycloalkyl, amino, substituted amino, aryl, aryloxy, carboxyl, carboxylalkyl, carboxyl(substituted alkyl), cyano, halo, nitro, heterocyclic, and trihalomethyl.

or a pharmaceutically acceptable salt thereof.

25. The compound of claim 24 wherein A_{12} is methylene or 1,1-ethanediyl and A_{13} is methylene.

26. The compound of claim 24 wherein R_{31} is hydrogen or methyl.

27. The compound of claim 24 wherein R_{32} is 2-morpholinoethyl, 2-(pyrrolidin-1-yl)ethyl, 4-piperidinylmethyl, 3-(*N,N*-dimethylamino)propyl, 2-(1-methylpyrrolidin-2-yl)ethyl, 2-(4-pyridyl)ethyl, or 3-(pyrrolidin-1-yl)propyl.

28. The compound of claim 1, which is a compound shown in Tables I-XI; or a pharmaceutically acceptable salt thereof.

29. A pharmaceutical composition comprising a compound as described in claim 1; and a pharmaceutically acceptable carrier.
30. A method of treating a disease or condition associated with sodium channel activity in a mammal, comprising administering to the mammal, a therapeutically effective amount of a compound as described in claim 1.
31. The method of claim 30 wherein the disease or condition is neuropathic pain.
32. A method of treating a disease or condition associated with sodium channel activity in a mammal, comprising administering to the mammal, a therapeutically effective amount of a pharmaceutical composition of claim 29.
33. The method of claim 32 wherein the disease or condition is neuropathic pain.